

Section II. Remarks**Amendment of the Specification**

In response to the objection to the specification at page 2 of the April 20, 2005 Office Action, noting that the priority application must be claimed in the first paragraph of the specification, it is pointed out that the priority claim already appears on the title page of the application, as follows:

Cross-Reference to Related Application:

This application claims priority under 35 USC § 119 of Korean Patent Application No. 10-2003-0062756 filed September 8, 2003

It therefore appears that the foregoing priority claim has been inadvertently overlooked in the examination of the application for compliance with formal requirements.

Nonetheless, to obviate this issue, and favorably conclude the examination of the application, the same wording as set out on the title page of the application has now been added immediately prior to the heading "BACKGROUND OF THE INVENTION" at page 1 of the specification.

The priority claim therefore has been set out in the application in the manner required by the examiner, and the specification accordingly is fully proper in form.

Rewriting of Claim 9 in Independent Form

In the May 10, 2005 Office Action, claim 9 was objected to as being dependent from a rejected independent claim. Claim 9 was otherwise not rejected on any reference or other formal grounds, although as originally submitted it depended indirectly (through intermediate claim 8) from claim 7, rejected, *inter alia*, on 35 USC §112, second paragraph grounds.

In response, claim 9 has been rewritten in independent form herein (including the amended recital overcoming the 35 USC §112, second paragraph rejection of claim 7; see discussion, *infra*).

Claim 9 is now in condition for allowance.

Cancellation of Claims 2, 5 and 16-17, Amendment of Claims 1, 3, 4 and 6-12, and Addition of New Claim 18; 35 USC §101 Rejection of Claims 16-17 and 35 USC §112, Second Paragraph Rejection of Claims 1-3, 5, 7, 8 and 17

Claims 2, 5 and 16-17 have been cancelled herein, claims 1, 3, 4, and 6-12 have been amended, and new claim 18 has been added.

The claims pending in the application are claims 1, 3-4, 6-15 and 18.

Apart from the amendment of claim 9 involving rewriting of such claim in independent form as discussed hereinabove, claims 1, 3, 4, and 6-12 have been amended herein, and same are now in condition for allowance.

Concerning the §101 rejection of claims 16 and 17, the same is moot in view of the cancellation of such claims.

Concerning the §112, second paragraph rejection of claim 1, such rejection is traversed for lack of stated basis for such rejection. Although claim 1 is identified together with claims 2, 3, 5, 7, 8 and 17 as being subject to rejection on §112, second paragraph grounds, at page 3 of the April 20, 2005 Office Action, there is no subsequent mention of claim 1 in the discussion of the specific grounds of the §112, second paragraph rejections, although all other first-mentioned claims (in line 1 of page 3) are mentioned with an elaboration of the reason for §112, second paragraph rejection.

It therefore appears that claim 1 was erroneously included in the listing of claims intended by the examiner to be rejected on §112, second paragraph grounds, and it therefore is respectfully requested that the examiner now withdraw such rejection of claim 1.

It is pointed out that claim 1 has been amended herein to recite specific small heat shock proteins and the respective organisms from which they have been derived, consistent with the disclosure at pages 3-4 of the application, and that all sHSP acronyms have been elaborated in the claim.

The §112, second paragraph rejection of claim 2 has been rendered moot by the cancellation of such claim.

With the cancellation of claim 2 (from which claim 3 formerly depended), claim 3 has been correspondingly amended to depend from claim 1.

In claim 3, in response to the examiner's requirement that the names of the specific small heat shock proteins must be spelled out, claim 3 has been amended to recite "inclusion body-associated protein A, inclusion body-associated protein B, inclusion body-associated protein AB, and heat shock protein 26."

Claim 4 has been amended to recite sHSP species and corresponding organisms in the same manner as amended claim 1.

The §112, second paragraph rejection of claim 5 has been rendered moot by the cancellation of such claim.

With the cancellation of claim 5 (from which claim 6 formerly depended), claim 6 has been correspondingly amended to depend from claim 4.

Concerning the §112, second paragraph rejection of claim 7, the terms of the claim cited in the rejection, viz., "protein mixture" and "increased number of spots," are submitted to be fully clear and definite as used in the claim, but to expedite the prosecution the former term has been amended to a recital of "mixture comprising a combination of different proteins" consistent with the examiner's proposed wording, and the latter term has been augmented with an express recital of what was implicit in the prior wording of the claim, by the recital of "increased number of spots as compared to a gel obtained for a corresponding mixture lacking said at least one small heat shock protein."

Further, in response to the examiner's requirement that the name of the sHSPs in claim 7 must be spelled out, claim 7 has been amended to set out the names of the sHSP species.

Claim 8 has been amended to delete the Table 1 reference objected to by the examiner, and such claim has been amended to recite the increased number of spots in claim 7 as being "at least 50%

more spots than the gel obtained for the corresponding mixture lacking said at least one small heat shock protein," consistent with the examiner's request for such numeral quantitation.

Claim 9 has been amended by rewriting same in independent form, and all sHSP acronyms have been elaborated in such claim.

Claims 10 and 11 have been amended in minor grammatical respects not affecting the substance of such claims.

Claim 12 has been amended to recite "combination of different proteins," consistent with the amendment of claim 7, from which claim 12 depends.

Claims 13-15 have been retained without change.

Claims 16 and 17 have been cancelled, as noted hereinabove.

New independent claim 18 has been added, which is of similar form to claim 9 as rewritten and indicated in the April 20, 2005 Office Action to be free of the art, but reciting the small heat shock protein (sHSP) as being derived from the selection group of organisms specified in Table 1 at pages 3-4 of the application.

No new matter (35 USC 132) has been added.

Rejection of Claims on Reference Grounds, and Traversal Thereof

In the April 20, 2005 Office Action, claims 1-8 and 10-17 as then pending were rejected on various reference grounds, including:

- a rejection of claims 1, 2, 4, 5, 7, 8, 10, 11, 16 and 17 under 35 USC §102(b) as anticipated by Willsie et al. ("Willsie");
- a rejection of claims 1-6 under 35 USC §102(b) as anticipated by Kitagawa et al. ("Kitagawa");

- a rejection of claim 15 under 35 USC §103(a) as unpatentable over Lubman et al. (“Lubman”); and
- a rejection of claims 7 and 12-14 under 35 USC §103(a) as unpatentable over Willsie in view of Kitagawa.

These rejections are traversed, in application to claims claims 1, 3-4, and 6-15 as amended and now pending in the application, based on the following remarks.

The 35 USC §102(b) Rejection of Claims 1, 2, 4, 5, 7, 8, 10, 11, 16 and 17 Over Willsie

Concerning the §102(b) rejection of claims 1, 2, 4, 5, 7, 8, 10, 11, 16 and 17, claims 2, 5, 16 and 17 have been cancelled, and the remaining claims 1, 4, 7, 8, 10 and 11 are patentably distinguished over Willsie.

“Anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration.” *W.L. Gore & Assocs. v. Garlock*, 721, F.2d 1540, 220 USPQ 303 at 313 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

Willsie fails to teach or suggest the specific small heat shock proteins that are recited in applicants’ independent claims 1, 4, and 7, which are specific in each instance to a source organism, and that are required in dependent claims 8, 10 and 11, each of which depends from independent claim 7.

Willsie instead discloses that brine shrimp small heat shock protein/α-crystalline protein p26 undergoes nuclear translocation in response to stress, e.g., heat shock or anoxia, in encysted embryos of *Artemia franciscana* and associates with HSP70 in the nuclear matrix.

Since all of the pending claims require small heat shock proteins of specific type as derived from a specifically recited source organism in each instance, none of which is disclosed in Willsie, Willsie fails to teach all of the limitations of claims 1, 4, 7, 8, 10 and 11.

Accordingly, Willsie cannot anticipate these claims 1, 4, 7, 8, 10 and 11, and withdrawal of the rejection thereof is respectfully requested.

The 35 USC §102(b) Rejection of Claims 1-6 Over Kitagawa

Concerning the §102(b) rejection of claims 1-6, claims 2 and 5 have been cancelled, and the remaining claims 1, 3, 4 and 6 are patentably distinguished over Kitagawa.

Kitagawa discloses heat shock protein constructs His-IbpA and His-IbpB including a polyhistidine tag, as fusion protein products made by subcloning IbpA and IbpB genes into expression vectors, as described in the paragraph bridging pages 2908 and 2909 of Kitagawa. The fusion protein constructs were found to protect enzymes from inactivation by heat, freeze-thawing and oxidation.

The heat shock fusion protein constructs His-IbpA and His-IbpB of Kitagawa are fusion molecules in which the His moiety is covalently bonded to IbpA or IbpB. Kitagawa therefore fails to teach the compositions of applicants' claims 1, 3, 4 or 6, in which the recited sHSP species are isolated species *per se*, not fusion constructs covalently bonded to other chemical moieties.

Since Kitagawa fails to teach or suggest the specific compositions that are recited in applicants' independent claims 1, 3, 4, and 6, Kitagawa cannot anticipate these claims 1, 3, 4 and 6, and withdrawal of the rejection thereof is respectfully requested.

The 35 USC §103(a) Rejection of Claim 15 Over Lubman

Concerning the §103(a) rejection of claim 15 based on Lubman, claim 15 recites "[A] method for the analysis of proteomes by 2-D gel electrophoresis, which is characterized by using the composition of claim 1."

The composition of claim 1 has been discussed hereinabove as regards the specific small heat shock proteins and source organisms recited in such claim.

Lubman discloses an automated system for separation and purification of proteins samples. This published patent application discloses only a single mention of heat shock protein in the

disclosure that "Some of the proteins found in the human erythroleukemia cell lysate ... heat shock protein (HS27) (Fuqua et al., *Cancer Research* 49:4126 [1989]), have been linked to various forms of cancer." There is no teaching or suggestion in Lubman of applicants' claim 15 recited method of "using the composition of claim 1" in "the analysis of proteomes by 2-D gel electrophoresis," with the composition of claim 1 being a "composition for preventing protein degradation," including isolated small heat shock proteins. Lubman by contrast only discloses that HS27 is present in human erythroleukemia cell lysate, as one of many components in the cell lysate mixture. There is accordingly no basis in Lubman for applicants' degradation preventing composition of claim 1, or the use of such a composition in performing proteomic analysis.

Accordingly, a *prima facie* case of obviousness is not present.

According to MPEP 2142:

To establish a *prima facie* case of obviousness, *three* basic criteria *must* be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Since Lubman fails to disclose all of the features of claim 15, and provides no basis that is suggestive or extrapolative of the applicants' method as recited in such claim, Lubman does not support a *prima facie* case of obviousness. Accordingly, withdrawal of the rejection of claim 15 under 103(a) is respectfully requested.

The 35 USC §103(a) Rejection of Claims 7 and 12-14 Over Willsie in View of Kitagawa

Concerning the §103(a) rejection of claims 7 and 12-14 based on Willsie in view of Kitagawa, claim 7, from which the other rejected claims 12-14 depend, recites, *inter alia*,

"[a] method for the 2-D gel electrophoresis of a mixture comprising a combination of different proteins, said method comprising:

adding at least one small heat shock protein (sHSP) to the mixture, so as to prevent protein degradation and obtain a gel with an increased number of spots as compared to a gel obtained for a corresponding mixture lacking said at least one small heat shock protein, wherein said at least one sHSP is selected from the group consisting of ... [the specified small heat shock proteins]."

Willsie, as already been discussed above, discloses that brine shrimp small heat shock protein/α-crystalline protein p26 undergoes nuclear translocation in response to stress, e.g., heat shock or anoxia, in encysted embryos of *Artemia franciscana* and associates with HSP70 in the nuclear matrix. Since claim 7 requires small heat shock proteins of specific type as derived from a specifically recited source organism in each instance, none of which is disclosed in Willsie, Kitagawa has been cited for its teachings of small heat shock proteins, the asserted motivation for combination of the two references being that "small heat shock proteins help to stabilize other proteins and remain associated with unfolded proteins in 2-D gel electrophoresis" (page 6, April 20, 2005 Office Action).

Contrariwise, however, there is no motivation for the applicants' claimed invention of independent claim 7, since, as already pointed out hereinabove, the small heat shock proteins of Kitagawa are heat shock protein constructs His-IbpA and His-IbpB including a polyhistidine tag, which are fusion protein products made by subcloning IbpA and IbpB genes into expression vectors, as described in the paragraph bridging pages 2908 and 2909 of Kitagawa.

The heat shock fusion protein constructs His-IbpA and His-IbpB of Kitagawa are fusion molecules in which the His moiety is covalently bonded to IbpA or IbpB. Kitagawa therefore lacks any disclosure of the compositions of applicants' claim 7, since applicants' claim 7 compositions are constituted by isolated sHSP species per se, not fusion constructs in which such species are covalently bonded to other chemical moieties.

The asserted motivational basis for combining Willsie and Kitagawa is further defeated, apart from the absence of any basis in either Willsie or Kitagawa for the small heat shock proteins recited in claim 7, by the fact that Kitagawa's fusion protein constructs were found to protect enzymes from inactivation by heat, freeze-thawing and oxidants - conditions that are logically carried out prior to conducting 2-D gel electrophoresis, and that are logically avoided in the 2-D gel electrophoresis process itself.

There is in this respect no indication that the 2-D gel electrophoresis process in Willsie is carried out at elevated heat shock temperature, freezing-thawing temperature, or under oxidative attack conditions, and no logical reason why it would be, so that there is no motivation whatsoever for protecting the homogenates of the encysted brine shrimp embryos of *Artemia franciscana* during 2-D gel electrophoresis by adding the fusion protein constructs His-IbpA and His-IbpB of Kitagawa to such homogenates, but even if there were, Willsie's homogenate already has endogenous heat shock proteins that "play a role in the protection of nuclear lamins within the nuclear matrix. Since the nuclear matrix proteins are already protected, there is no tenable reason for the addition of Kitagawa's fusion protein constructs His-IbpA and His-IbpB, but even if there were, the resulting "mix" would still not contain the specific sHSP species required by claim 7, and as a result of their dependence, by claims 12-14 depending from claim 7.

In sum, there is no objective teaching or basis in either of the references for the proposed hypothetical combination of Willsie and Kitagawa. No *prima facie* case of obviousness is present for the rejection of claim 7.

As was stated by the Board of Patent Appeals and Interferences in *Ex parte Obukowicz*, 27 U.S.P.Q. 2d 1063, 1065 (B.P.A.I. 1992):

"In proceedings before the Patent and Trademark Office, the examiner bears the burden of establishing a *prima facie* case of obviousness based upon the prior art....The examiner can satisfy this burden only by showing some objective (emphasis added) teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teaching of the references."

Here the objective teachings of the references and knowledge of the art provide no motivational basis for combining Willsie and Kitagawa in the proposed manner, and even if the references

were to be combined in such fashion, the resulting combination would still not yield the applicants' claimed invention, since the combination would still lack the specific heat shock proteins of applicants' claimed invention.

On such basis, it is respectfully requested that the rejection of claims 7 and 12-14 be withdrawn.

Payment of Fee for Rewriting of Claim 9 in Independent Form

The rewriting of claim 9 herein in independent form, and the addition of new independent claim 18 herein, with the cancellation of independent claim 16 herein, increases the number of independent claims by one, beyond the number for which payment previously has been made. Accordingly, an added claims fee of \$100 is payable. Payment is enclosed in the form of a credit card authorization form authorizing payment in the amount of \$160 as inclusive of such added claims fee of \$100 and the amount of the fee for the one month extension of the term for response to the April 20, 2005 Office Action (see *infra*).

Authorization also is given to charge any additional fee or amount that may be properly payable in connection with the filing and entry of this response, to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

Petition Under 37 CFR 1.136 for One Month Extension of Term for Response

Petition hereby is made under the provisions of 37 CFR 1.136 for a one month extension of the term for response to the April 20, 2005 Office Action, to August 22, 2005. Payment for such extension of the term for response is enclosed in the form of a credit card authorization form authorizing payment in the amount of \$160 as inclusive of the fee for the one month extension of the term for response to the April 20, 2005 Office Action, as well as the added claims fee of \$100 specified in the preceding discussion.

Authorization also is given to charge any additional fee or amount that may be properly payable in connection with the filing and entry of this Response, to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

CONCLUSION

The pending claims 1, 3-4, 6-15 and 18 of the application are now in form and condition for allowance.

If any issues remain outstanding, incident to the formal allowance of the application, the examiner is requested to contact the undersigned attorney at (919) 419-9350 to discuss their resolution, in order that this application may be passed to issue at an early date.

Respectfully submitted,



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